

Effect of CHX (Chlorexidine) in Preventing SARS COVID 2

Dr. Bomma Vijayani¹, Dr. Surapaneni Bhavana²

Abstract: *Considered to be a major portal of entry for infectious agents, the oral cavity is directly associated with the evolutionary process of SARS-CoV-2 in its inhalation of ambient particles in the air and in excretions. Some new generations of mouth rinses currently on the market have ingredients that could contribute to lower the SARS-CoV-2 viral load, and thus facilitate the fight against oral transmission. Chlorhexidine (CHX) is a widely used antimicrobial agent in dentistry. Herein, we report the synthesis of a novel mesoporous silica nanoparticle-encapsulated pure CHX (Nano-CHX), and its mechanical profile and antimicrobial properties against oral biofilms.*

Keywords: Chlorexidine CHX, SARS COVID-2, mouthwash, pneumonia, OHC

1. Introduction

The epidemic of infection COVID-19 (or 2019-CoV) by an emerging coronavirus SARS-CoV-2 in December 2019 has generated severe threats to international health security, global health, and the economy. The genome of COVID-19 is a single-stranded positive-sense RNA. The sequence analysis showed that the COVID-19 possessed a typical genome structure of coronavirus and belonged to the cluster of β -coronaviruses including SARS-CoV and MERS-CoV. COVID-19 was more than 82% identical to those of SARS-CoV. COVID-19 may spread worldwide with the pandemic. Currently, there is no registered treatment or vaccine for the disease. Given the current lack of effective treatment there is a need to explore alternative methods to contain the propagation of the infection, focusing in particular on its mode of transmission.

The person-to-person modes of transmission of SARS-CoV-2 are direct transmissions, such as sneezing, coughing, transmission through inhalation of small droplets, and transmission by contact such as contact with nasal, oral, and ocular mucous membranes, as well as transmission through asymptomatic subjects. SARS-CoV-2 may also be transmitted directly or indirectly by the saliva, and the fetal-oral routes can be a possible route of person-to-person transmission as well. Moreover, In ventilator associated pneumonia, high viral loads have been found in the oropharynx of infected patients. The oral cavity is therefore directly associated with the evolutionary process of SARS-CoV-2 in its inhalation of ambient particles in the air and in excretions.

The oral cavity and nasopharyngeal regions can be considered as the anatomical transition between external and internal environments. The standard oral cavity temperature is on average 37 °C with no notable variations, which gives the microorganisms a secure environment to survive. Saliva is also pH stable at 6.5–7, which is the favorable pH to oral microbiota (bacteria species and virus such as coronavirus).

Patient Specimens

In Hong Kong, 2019-nCoV testing was performed by Public Health Laboratory Services Branch in Hong Kong for patients who fulfilled the reporting criteria or enhanced

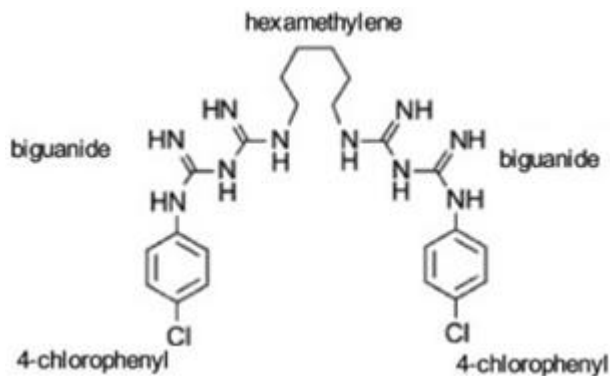
surveillance criteria. A patient is considered to have laboratory-confirmed infection if 2019-nCoV was detected in their nasopharyngeal or sputum specimens.

Saliva was collected by asking the patient to cough out saliva from their throat into a sterile container, and 2 mL of viral transport medium was added as we described previously. This study was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster.

Oral microbiota comprises of commensal bacterial populations that sustain mutual benefits with the host and keep potentially pathogenic bacteria in balance through a number of negative feedback mechanisms. In the oral biofilm, these bacteria combine to make a barrier which resists to antibiotics, disinfectants, mechanical removal, and other stresses. Moreover, in biofilms, bacteria can escape the immune system producing so-called superantigens. In addition to host-microbe interactions, the interfaces of periodontal pathogens with other non-host pathogens, such as herpesviruses like Epstein-Barr virus and cytomegalovirus, can contribute to the pathogenesis of the periodontal disease, or can affect the outcome of viral infection and dissemination. These risks are often significantly underestimated.

Chlorexidine

Effective ingredients that may be applied in therapeutic mouth rinses includes: chlorhexidine (CHX), fluoride, cetylpyridinium chloride, essential oils, and peroxide. Conceived for short-term usage, CHX 2% is a cationic bis-biguanide widely used in general medical practice as a broad-spectrum antiseptic. CHX increases the permeability of the bacterial cell wall, resulting in bacterial lysis.



Its activity includes gram-positive and gram-negative bacteria (gram-positive bacteria being more susceptible), aerobes, facultative anaerobes, fungi, and selected viruses. While chlorhexidine significantly reduces the risk of ventilator-associated pneumonia, no differences were found in terms of mortality, mechanical ventilation, or length of stay in the intensive care unit. However, and of major importance for the care of ventilator-associated COVID-19 patients, several drawbacks have been cited i.e., a reduced susceptibility to CHX of number of ventilator-associated pneumonia pathogens and an increased risk of death in the less severe patients. In oral health, it is commonly accepted that a preoperative antimicrobial mouth rinse decreases the number of oral pathogens. One of the more common CHX indications are gingivitis, periodontitis, post-surgery periodontal disease, and implantology. While CHX at lower concentrations is bacteriostatic, at higher concentrations it also has a bactericidal effect. CHX has been reported to penetrate the oral biofilms as well, affecting their growth or directly having a bactericidal impact.

The release of CHX from the Nano-CHX was characterized by UV/visible absorption spectroscopy. The antimicrobial properties of Nano-CHX were evaluated in both planktonic and biofilm modes of representative oral pathogenic bacteria. The Nano-CHX demonstrated potent antibacterial effects on planktonic bacteria and mono-species biofilms at the concentrations of 50–200 µg/mL against *Streptococcus mutans*, *Streptococcus sobrinus*, *Fusobacterium nucleatum*, *Aggregatibacter actinomycetemcomitans* and *Enterococcus faecalis*. Moreover, Nano-CHX effectively suppressed multi-species biofilms such as *S. mutans*, *F. nucleatum*, *A. actinomycetemcomitans* and *Porphyromonas gingivalis* up to 72 h.

Bacterial species	Planktonic mode	Mono-species biofilms
<i>S. mutans</i>	50	100**
<i>S. sobrinus</i>	100	200*
<i>F. nucleatum</i>	50	100**
<i>A. actinomycetemcomitans</i>	50	100**
<i>E. faecalis</i>	100	200*

Significant difference from the planktonic mode,
 * $p < 0.05$,
 ** $p < 0.01$.
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CHX nanoparticles have the potential to inhibit the development of a multi-species oral biofilm made up of

Porphyromonas gingivalis, *Streptococcus sobrinus*, and *Fusobacterium nucleatum*.

2. Results

High quality evidence from 18 RCTs (2451 participants, 86% adults) shows that CHX mouthrinse or gel, as part of OHC, reduces the risk of ventilator associated pneumonia which is indeed associated again with sars-covid-2 compared to placebo or usual care from 24% to about 18% (RR 0.75, 95% confidence intervals (CI) 0.62 to 0.91, $P = 0.004$, $I^2 = 35\%$). This is equivalent to a number needed to treat for an additional beneficial outcome (NNTB) of 17 (95% CI 9 to 50), which indicates that for every 17 ventilated patients in intensive care receiving OHC including chlorhexidine, one outcome of VAP directed to sars-covid-2 would be prevented. There is no evidence of a difference between CHX and placebo/usual care for the outcomes of mortality (RR 1.09, 95% CI 0.96 to 1.23, $P = 0.20$, $I^2 = 0\%$, 14 RCTs, moderate quality evidence), duration of mechanical ventilation (MD -0.09 days, 95% CI -1.73 to 1.55 days, $P = 0.91$, $I^2 = 36\%$, five RCTs, 800 participants, low quality evidence), or duration of intensive care unit (ICU) stay (MD 0.21 days, 95% CI -1.48 to 1.89 days, $P = 0.81$, $I^2 = 9\%$, six RCTs, 833 participants, moderate quality evidence).

3. Conclusion

OHC including chlorhexidine mouthwash or gel reduces the risk of developing ventilator-associated pneumonia in critically ill patients from 24% to about 18%. However, there is no evidence of a difference in the outcomes of mortality, duration of mechanical ventilation or duration of ICU stay. Nano-CHX may be developed as a novel and promising anti-biofilm agent for clinical use.

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Authors

Dr. Bomma Vijayani.

Dr. Surapaneni Bhavana.

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